PATENT 671308-2001.1

AMENDMENTS IN THE CLAIMS

Please amend the claims without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows:

- 1. (Original) A method for delivering a gene in a system for delivering DNA specifically to tumor tissues under anaerobic conditions, wherein a bacterium belonging to the genus *Bifidobacterium* is used as a gene delivery vector and then the DNA delivered specifically to tumor tissues under anaerobic conditions is expressed in said tumor tissues.
- 2. (Original) A method for delivering a gene in a system for delivering DNA specifically to tumor tissues under anaerobic conditions, wherein a bacterium belonging to the genus *Bifidobacterium* and having the DNA coding for a protein which has a higher activity than in its parent strain is used as a gene delivery vector and then the DNA delivered specifically to tumor tissues under anaerobic conditions is expressed in said tumor tissues.
- 3. (Original) A method for delivering a gene in a system for delivering DNA specifically to tumor tissues under anaerobic conditions, wherein a bacterium belonging to the genus *Bifidobacterium* transformed with a recombinant DNA having said DNA is used as a gene delivery vector and the DNA delivered specifically to tumor tissues under anaerobic conditions is expressed in the tumor tissues.
- 4. (Original) The method as claimed in any one of Claims 1 to 3, wherein the DNA is selected from the group consisting of:
- (a) DNA coding for a protein having an antitumor activity, and
- (b) DNA coding for a protein having an activity of converting a precursor of an antitumor substance into the antitumor substance.
- 5. (Original) The method as claimed in Claim 4, wherein the protein having an antitumor activity is interleukin-2.
- 6. (Original) The method as claimed in Claim 4, wherein the precursor of an antitumor substance is selected from the group consisting of 5-fluorocytosine, 5-aziridino-2,4-dinitrobenzamide, ganciclovir, a glucuronic acid-conjugated antitumor substance and a lysine-conjugated antitumor substance.
- 7. (Original) The method as claimed in Claim 4, wherein the protein having the activity of converting a precursor of an antitumor substance into the antitumor substance is a protein



PATENT 671308-2001.1

selected from the group consisting of cytosine deaminase, nitroreductase, herpes simplex virus type 1 thymidine kinase and β -glucuronidase.

- 8. (Original) The method as claimed in Claim 3, wherein the recombinant DNA is an expression vector.
- 9. (Original) The method as claimed in Claim 8, wherein the expression vector has a promoter and a terminator functioning in a bacterium belonging to the genus *Bifidobacterium*.
- 10. (Original) The method as claimed in Claim 9, wherein the promoter and terminator are those involved in expressing a gene coding for histone-like DNA-binding protein (HU protein) derived from *Bifidobacterium longum*.
- 11. (Original) The method as claimed in Claim 9, wherein the promoter and terminator are DNAs located at the 1- to 192-positions and at the 472- to 600-positions respectively in the nucleotide sequence set forth in SEQ ID NO: 1.
- 12. (Currently amended) The method as claimed in any one of Claims 1 to 11-3, wherein the bacterium is *Bifidobacterium longum*.
- 13. (Currently amended) The method as claimed in any one of Claims 1 to 4 or 6 to 12-3, wherein the bacterium is *Bifidobacterium longum* 105-A/pBLES100-S-eCD (FERM BP-7274).
- 14. (Currently amended) A method for expressing a gene coding for a protein having an antitumor activity in tissue tumors specifically, which comprises use of the bacterium as claimed in any one of Claims 1 to 5 or 8 to 12 3.
- 15. (Currently amended) A method for expressing a gene coding for a protein having the activity of converting a precursor of an antitumor substance into the antitumor substance in tissue tumors specifically, which comprises use of the bacterium as claimed in any one of Claims 1 to 4 or 6 to 12 3.
- 16. (Currently amended) A pharmaceutical composition comprising the bacterium as claimed in any one of Claims 1 to 13-3.
- 17. (Currently amended) The pharmaceutical composition as claimed in Claim 16, wherein the pharmaceutical composition comprises a combination of the bacterium as claimed in any one of Claims 1 to 4 or 6 to 13 and further comprising the precursor of an antitumor substance.

PATENT 671308-2001.1

- 18. (Currently amended) The pharmaceutical composition as claimed in Claim 16, wherein the pharmaceutical composition comprises the bacterium as claimed in any one of Claims 1 to 4 or 6 to 13 and further comprising the precursor of an antitumor substance.
- 19. (Currently amended) The pharmaceutical composition as claimed in any one of Claims Claim 16 to 19, wherein the bacterium is Bifidobacterium longum.
- 20. (Currently amended) The pharmaceutical composition as claimed in any one of Claims Claim 16 to 19, wherein bacterium is *Bifidobacterium longum* 105-A/pBLES100-S-eCD (FERM BP-7274).
- 21. (Currently amended) A bacterium belonging to the genus *Bifidobacterium*, which is used in the method as claimed in any one of Claims 1 to $\frac{13-3}{2}$.
- 22. (Original) Bifidobacterium longum 105-A/pBLES100-S-eCD (FERM BP-7274.
 - 23. (Original) DNA having the nucleotide sequence set forth in SEQ ID NO: 1.
- 24. (Currently amended) A method of treating a solid tumor, which comprises use of the method as claimed in any one of Claims 1 to 15-3.
- 25. (Currently amended) A method of treating a solid tumor, which comprises administering the bacterium as claimed in any one of Claims 1 to 4 or 6 to 13 in combination with the precursor of an antitumor substance.
- 26. (Original) An anaerobic bacterium belonging to the genus *Bifidobacterium* capable of expressing a gene coding for a protein having an antitumor activity in only cancer cells under substantially anaerobic conditions.
- 27. (Original) An anaerobic bacterium belonging to the genus *Bifidobacterium* capable of expressing a gene coding for a protein having the activity of converting a precursor of an antitumor substance with low toxicity to humans and animals into an antitumor substance in only cancer cells under substantially anaerobic conditions.

